Liver, Hepatocyte – Necrosis, single cell

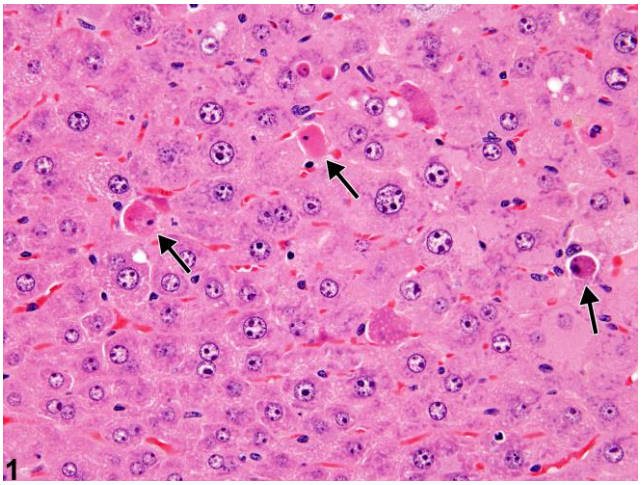

Figure Legend: Figure 1 Single-cell necrosis (arrows) in a male B6C3F1 mouse from subchronic study.

Comment: Single-cell necrosis (Figure 1, arrows) represents one form of cell death, and some consider it synonymous with apoptosis. Necrosis of individual nonconfluent hepatocytes occurs spontaneously or following exposure to hepatotoxic xenobiotics. Affected cells have condensed, deeply eosinophilic cytoplasm in contrast to adjacent normal hepatocytes and may contain pyknotic nuclei or fragmented nuclear material. When affected, hepatocytes may be rounded and surrounded by a clear halo (Figure 1). This change is morphologically compatible with an apoptotic body. The more angular profiles of hypereosinophilic hepatocytes represent early stages of single-cell necrosis prior to development of more classical features of apoptosis. Apoptosis is considered a form of single-cell necrosis, but a diagnosis of apoptosis requires definitive identification using specific immunohistochemical staining or electron microscopy. Single-cell necrosis can also be found at the peripheral edges of some regions of confluent coagulation necrosis. The example of single-cell necrosis in Figure 1 is associated with microsomal enzyme induction and has a centrilobular pattern of distribution.

Recommendation: It is necessary to distinguish single-cell necrosis from examples of confluent necrosis when comparing studies and characterizing response to treatment. A potential exception would be when frank confluent necrosis occurs at high doses but single-cell necrosis with a similar lobular distribution pattern is seen at low doses with the same xenobiotic

and within the same study. In such a case, it is likely that the process is the same and using separate diagnoses would inappropriately misrepresent the continuum of that process. Such a scenario would require clear explanation in the pathology narrative. It is recommended that single-cell necrosis be given a severity grade based on its frequency of occurrence.

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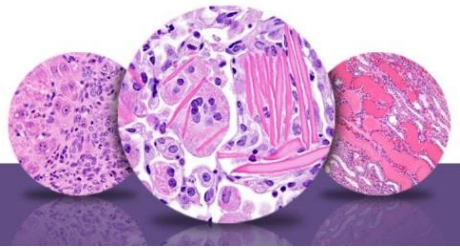

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Author:

Robert R. Maronpot, DVM, MS, MPH, DACVP, DABT, FIATP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC